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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,866	06/04/2001	Mark K. Hechinger	1007-103.US	4668

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COLIN P ABRAHAMS
5850 CANOGA AVENUE
SUITE 400
WOODLAND HILLS, CA 91367

EXAMINER

CHEU, CHANGHWA J

ART UNIT PAPER NUMBER

1641

DATE MAILED: 09/22/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/873,866

Applicant(s)

HECHINGER, MARK K.

Examiner

Jacob Cheu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 20-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on June 27, 2003 has been received and entered into record and considered.

Claim Rejections - 35 USC § 112

Written Description

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-19 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to claims 1, 14 and 15, applicant recites the surfactancy is no more than 0.5% v/v of the beads. However, there is no support from the specification, particularly on the unit v/v. Therefore, the recited limitation lacks a clear written description support. Similarly, the newly amended 0.5% v/v limitation also constitutes new matter.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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With respect to claim 12, "RNP/SM, SM, SS-A, SS-B, SCL-70 and dsDNA" is vague and indefinite. Applicant needs to clearly specify each of the recited substance.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1, 5-11, 13-19 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen Peter. (USP 5286452) in view of Bignami et al. (USP 5118607)

Hansen teaches preparing immunoassay beads in a physiological buffer, i.e. HEPES. (Col. 13, line 54-55) Hansen also teaches selecting size of beads around coefficient of variation of diameter of particles ranged from 0.1- 4.0% to reduce surfactancy of the beads. (Col. 13, line 55-58) In addition, Hansen teaches that both Ag or Ab proteins could be coated on the beads for detection purpose. (Col. 2, line 24-26) Hansen teaches incubate the bead-antibody mixture with the buffer. (Col. 13, line 52-59) Hansen teaches using protein to block the non-specific binding

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sites on the beads, i.e. 0.1% or 0.5 BSA (Col. 13, line 67; Col. 14, line 48) Furthermore, Hansen teaches the sizes of the particles ranging from 0.02 to 12 μm and using multiple-size beads for simultaneous assay. (Col. 12, line 25-40; Example 4) Hansen teaches detecting cellular antigens in human serum such as thyroid stimulating hormone (TSH). (Col. 14, line 35-40) Hansen also teaches prewashing bead buffer, centrifuging, vortexing and resuspension of the coated beads. (See Example 1, 2) However, Hansen et al. do not teach reducing the surfactancy of the beads to no more than 0.5% v/v to allow antigens to the beads.

Bignami et al. teach adding surfactants to the solvent system for detecting analytes in interest because it has been shown that adding surfactants can reduce the amount of non-specific binding or the signal to noise ratio.(Col. 2, line 47-56) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided the method of Hansen et al. with the surfactants as taught by Bignami et al. to provide a better antigen-bead binding environment since addition of the surfactant offering the advantage in reducing the amount of non-specific binding or signal to noise ratio.

With respect to the limitation of “no more than 0.5 % v/v” of surfactant, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have the recited limitation, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)

6. Claims 2, 3, 4 are rejected under 35 U.S.C. 103 (a) as unpatentable over Hensen in view of Bagnami et al., as applied to claim 1 above, and further in view of Fulwyler et al. (Method in Cell Biology, Vol. 33, Ch. 15 (1990) Page 613-629)

Both Hensen and Bignami et al. references have been discussed before but do not explicitly teach using carbonate buffer for the coating process. Fulwyler et al. teach coating microparticles in flow cytometers for detection of analyte of interest. Fulwyler et al. teach that the coating process is dependent on the pH and the ionic strength of the

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buffer. (page 617, First paragraph) Fulwyler et al. teach using sodium bicarbonate buffer (pH = 9.5) for better noncovalent protein attachment of the microparticles. (See VI Appendix: Solutions and Suppliers) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided the methods of Hansen and Bignami et al. with the agent of carbonate buffer as taught by Fulwyler et al., for better adsorption of the antigens on the microparticles in the flow cytometer assay.

7. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen in view of Bignami et al., as applied to claim 1 above, and further in view of Lim et al. (Chemical Sensor (1998) 14: 77-80) (*English Abstract*)

Both Hensen and Bignami et al. references have been discussed but fail to specifically teach using specific antigens as recited in this application, such as rheumatic diseases proteins, i.e. dsDNA, SS-B, SS-A or Scl-70. Lim et al. teach using automated flow immunoassay as a simple, rapid, and convenient method, to detect rheumatic related antibody dsDNA. (See abstract) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided the assay method of Hansen and Bignami et al. to detect rheumatic disease proteins as taught by Lim et al. since using flow cytometer to detect cellular antigen or antibody is a routine clinical practice in the art for a simple, convenient and rapid analysis.

Response to Applicant's Arguments

8. Applicant's arguments with respect to claims 1-19 and 26 have been considered but are moot in view of the new ground(s) of rejection.

With respect to Hansen et al. reference, applicant argues that the instant invention differs from the teachings of Hansen et al. because of its specific sequentially relevant method as compared to that of the Hansen et al. (See page 14, third paragraph, Amendments filed on June

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27, 2003) The arguments have been considered but are not persuasive. The instant invention of making a bead for immunoassay comprising there main steps in sequence, namely adding an antigen to the beads, where the beads have been selected according to size and treated with surfactants, form bead-antigen complex, then add buffer, and finally add bovine serum albumin to reduce non-specific binding. (See claim 1) The Hansen et al. reference encompassing the three main steps, including incubating the beads, where the beads have been selected according to size only, with antibody, and then finally add bovine serum albumin to reduce non-specific binding. (Col. 13, line 50-65) Hansen et al. also teach that both antibody or antigen could be coated on the particles for detection purposes. (Col. 2, line 22-32) Therefore, there is no difference of sequence/or procedure in terms of preparing the beads for immunoassay.

With respect to Fulwyler et al. reference, applicants argues (1) no preincubation in Fulwyler et al. is required; (2) no 37 degree incubation for 1 h for blocking is required; (3) no storage of beads in solution containing glycerol is required; (4) no washes between incubation steps. The arguments have been considered but are not persuasive because applicant does not recite these limitations in claim language. With respect to the arguments on using bicarbonate and carbonate *mixtures* for the buffer, the argument is considered but is not convincing. First there is no support in the claim reciting that the invention uses both bicarbonate and carbonate mixture. Applicant only recites carbonate. Second, using bicarbonate/or carbonate to adjust pH in the buffer is a common practice in the art, and only involves ordinary skill. Third, the purpose of using carbonate/or bicarbonate is for adjusting pH, and Fulwyer et al. teach using pH= 9.5 falls within the recited claim range.

Conclusion

8. No claim is allowed.

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Jacob Cheu
Examiner
Art Unit 1641



September 17, 2003



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

8-9/19/03